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PHYSIOLOGICAL NOTES

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HARVARD MEDICAL SCHOOL
DEPARTMENT of PHYSIOLOGY.

NOTES

FROM THE

PHYSIOLOGICAL LABORATORY

OF THE

UNIVERSITY OF PENNSYLVANIA.

EDITED BY

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PREFACE.

THE papers which form this little volume are simply the brief records of facts of interest brought to light in the course of physiological study.

The constant aim of the writers has been to present these facts with the greatest conciseness compatible with scientific accuracy.

Judgment upon this and other qualities is, however, left to the friendly reader by

THE EDITORS.

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I.

A NOTE ON THE FÆCES OF STARCH-FED INFANTS.

THE series of experiments presented in the preceding paper by Dr. Keating seems to me to be in the highest degree suggestive, for it is only rational to suppose that the development of the amylolitic ferment of the pancreatic juice is coincident with the appearance of the analogous salivary ferment.[1] Inasmuch, however, as the food even in spoon-fed infants is retained but a short time in the mouth, and further, as the continued action of the saliva after it enters the stomach is as yet problematical, the only absolute control for such observations is afforded by an examination of the fæces.

Through the kindness of Dr. Keating I have been enabled to examine the stools of twenty-four starch-fed infants, of ages varying from forty-five days to eighteen months. Twenty-three of these children were fed upon cracker-dust, water, and

[1] The experiments in question demonstrated the activity of the *saliva* of very young infants.

condensed milk. The twenty-fourth received corn-starch boiled in milk.

The freshly evacuated fæces of each infant were carefully bottled and labelled, and a drop of a solution of iodine was added to a small portion of each specimen, which was then submitted to microscopical examination. Besides turning the starch blue, and indicating the presence of dextrine by a peculiar mahogany-red color, the iodine has the advantage of rendering any fats which may be present much more readily apparent. The reaction of each specimen was taken, but though this varied from acid to alkaline and neutral, no correlation between the reactions and the other properties of the specimens could be observed. A decoction of each was tested for glucose with freshly-prepared Fehling's solution, but except in one instance no appreciable amount could be found.

The presence of *starch* was exceptional and apparently in no degree dependent upon the age of the child. The stools of eighteen out of the twenty-four children contained either no starch, or but a trace,—*i.e.*, no more than is frequent in the evacuations of a healthy adult upon a mixed diet. Six of these specimens were from children of three months or less,—the youngest being but forty-five

days old. In many cases the broken and empty cellulose envelopes of the starch-granules were clearly discernible.

The six infants in whose evacuations a noteworthy amount of starch was present were aged respectively three, four, ten, thirteen, fourteen, and seventeen months. The eldest two were in very bad health.

The following is a tabular statement of the age, diet, and appearances of the fæces in the children forming the subject of this study:

AN EXAMINATION OF THE FÆCES OF TWENTY-FOUR STARCH-FED INFANTS.

No.	Name.	Age.	Food.	Starch present.	Remarks.
1	Savin	45 days.	Condensed milk and cracker-dust.	None.	
2	Jocker.....	2 mos.	"	Traces.	
3	McGettinger.	2+ "	"	"	
4	McGowan.....	3 "	"	"	Twice examined: no fat before inunction, about 10 per cent. after.
5	Ross	3 "	"	"	
6	Hays.....	3 "	"	About ¼ starch.	
7	Soy.....	3 "	"	Traces.	
8	Henwich.....	4 "	Corn-starch and milk.	"	
9	Moore.....	4 "	Condensed milk and cracker-dust.	None.	Many broken cellulose envelopes.
10	Conway.....	4+ "	"	Traces.	Evidences of potato surreptitiously given.
11	Roach.....	5 "	"	About ½ starch.	
12	Anxier.....	5+ "	"	None.	
13	Schmitz...	5+ "	"	"	Many bacteria.
14	McKinley.....	6+ "	"	"	10 per cent. fat; had had inunctions.

AN EXAMINATION OF THE FÆCES—(*Continued*).

No.	Name.	Age.	Food.	Starch present.	Remarks.
15	Hall.....	8+ mos.	Breast and cracker-food.	Traces.	
16	Hensen.....	10+ "	Condensed milk and cracker-dust.	More than normal.	Many bacteria; evidences of potato surreptitiously given.
17	Devine.....	13— "	"	20 to 30 per ct.	Some glucose present and indications of dextrine; saliva was found to be inefficient.
18	Croncla.....	14— "	"	Traces.	
19	Madden.....	14 "	"	"	
20	Boyle.....	14 "	"	10 per ct. starch.	Sick.
21	Glass.....	14+ "	"	None.	Except a few large cells containing starch from potato.
22	Kinscher.....	17— "	"	"	
23	Wood.....	17— "	"	Over ¾ starch.	Syphilitic; saliva was found to be inefficient.
24	Dane.....	18 "	"	Traces.	Indications of dextrine.

The facts presented appear to justify the following conclusions:

First, that *many* infants of under three months can digest starchy foods;

Second, that the individual variations in this regard are so numerous that no broad and general statement can be made as to the period at which infants *begin* to digest starches; and,

Third, that the physician can be absolutely certain that a farinaceous ingredient in the diet of a young infant is beneficial only by an examination of the dejecta under such diet.

II.

AN EXAMINATION OF THE FÆCES OF TWENTY PERSONS RECEIVING INUNCTIONS OF COD-LIVER OIL.

In a study of the fæces of starch-fed infants[1] one of us observed a specimen in which there was present a very notable amount of oil-globules. Upon inquiry, it was found that the child in question had been receiving inunctions of cod-liver oil.

The same coincidence was a second time noted, and the following series of experiments was then instituted.

The fæces of fourteen infants, in fairly average health, were examined with negative results as far as oil was concerned, except in one case.

These infants were then thoroughly rubbed with cod-liver oil twice daily for eleven days, care being taken to cleanse the surface of the body after each

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[1] Randolph: Transactions of the College of Physicians of Philadelphia, 3d series, vol. vi. p. 443.

inunction, and the fæces of each examined for oil at the end of the third and of the eleventh day of inunction. At the end of the third day, traces of fat were observed in the majority of the specimens. On the eleventh day all but three specimens exhibited, on microscopical examination, a decidedly notable quantity of unabsorbed fat,—numerous oil-globules being apparent in every field.

In like manner an examination was made of the dejecta of six adults, after which each was twice daily well rubbed with cod-liver oil in the groins and axillæ for a period of three weeks. The fæces of the adults contained normally much more fat than those of the infants, but in all but one case there was a well-marked increase in the proportion of fatty globules at the end of the treatment.

The circumstances of the examination precluded the application of the ether method for the estimation of fats, and we were forced to rely upon a close microscopical examination. For the micrometric method only relative accuracy is claimed, and we hope soon to be able to go over the same ground, substituting a chemical for the optical method in the determination of fats. By the use, however, of well-mixed specimens, and by carefully averaging the contents of many fields from the same specimen,

we have obtained results which we believe accurately represent the changes in the *relative* proportion of fat in the specimens examined, although the unit assumed may not correspond with that obtained by gravimetric methods.

The individuals under observation were upon a diet practically uniform in composition and quantity, both before and during the treatment. At the end of the period of inunction a marked gain in weight and general health was noted in the majority of the cases.

The results of our study are indicated in the following tables:

No.	Age.	Diet.	Fat in Fæces before Inunction.	After Three Days' Inunction.	After Eleven Days' Inunction.
1	2 months.	Milk and crackers.	Negative.	Negative.	Negative.
2	3 "	" "	"	"	3 per cent.
3	4 "	" "	"	Traces.	3.5 " "
4	5 "	Corn-starch and milk.	"	"	5 " "
5	5 "	Milk and crackers.	"	"	3 " "
6	5 "	" "	"	Negative.	Negative.
7	6 "	" "	Traces.	Traces.	Traces.
8	6 "	" "	Negative.	Negative.	3.5 per cent.
9	8 "	" "	"	"	5 " "
10	11 "	" "	"	Traces.	3.5 " "
11	12 "	" "	"	"	3 " "
12	14 "	" "	"	"	3.5 " "
13	14 "	" "	"	"	2.5 " "
14	15 "	Corn-starch and milk.	"	"	3.5 " "

No.	Age.	Diet.	Fat in Fæces before Inunction.	Fat in Fæces after 21 Days' Inunction.
1.....	Adult.	Hospital Diet.	Traces.	Traces.
2.....	"	" "	2 per cent.	5+ per cent.
3.....	"	" "	2 " "	10+ " "
4.....	"	" "	3 " "	10 " "
5.....	"	" "	Negative.	Traces.
6.....	"	" "	"	"

It will be seen, from the tables given above, that in 80 per cent. of the cases a notable increase of the fatty matters passed per anum was observed after the persistent inunction of cod-liver oil. In the remaining 20 per cent. the quantity of fæcal fats was unaltered by the treatment, and in one case remained negative throughout.

We venture to suggest, as a provisional hypothesis, that by the continued inunction the circulating fluids became to some extent surcharged with fats, and that, in consequence, a certain amount of the fatty constituents of the food was refused by the absorbent surfaces of the intestine and passed from the body unaltered. This supposition is strengthened by the observations of Berthe,[1] who showed that pure cod-liver oil, given internally, could be taken for a longer time without appearing in the fæces,

[1] L'Union Médicale, t. x. No. 62, 1856.

than could an equal amount of butter or any of the other animal and vegetable fats.

We further suggest that, in practice, the increase of fat in the stools constitutes a physiological test for the efficiency of the aliptic treatment in the great majority of cases, and that by the application of this test both the frequency of exhibition and the amount of a remedy rather repugnant to the average patient may be reduced to the minimum necessary for efficient treatment.

III.

A STUDY OF THE DISTRIBUTION OF GLUTEN WITHIN THE WHEAT-GRAIN.

THE object of the present paper is to briefly describe several methods for the demonstration of gluten in the central portion of the wheat-grain, and the results of their application.

For many years the great majority of observers and of writers upon gluten have stated that this highly important nitrogenous element of food is found almost, if not quite exclusively, in the fourth layer (Parkes) of the grain, immediately below and adherent to the third or inner coat of the true bran. This fourth layer is composed of closely-packed yellowish granular cells of ovate or cuboid form, each of which is provided with a dense, laminated cellulose wall, and contains a large proportion of free fat. Immediately within this layer of so-called "gluten-cells," and constituting the greater portion of the grain, is an aggregation of much larger, usually elongated, cylindrical cells, whose contents are *appa-*

rently made up exclusively of starch-granules which exhibit great diversity in size.

So fixed and widespread has the belief become that the gluten of the wheat resides in specific cortical cells of the grain, that not only do many most intelligent persons habitually rasp their digestive surfaces with branny foods, but attempts to determine, by microscopical examination, the nutritive values of various prepared foods have been made, in which the proportion of "gluten-cells" found in a given food formed the criterion of its value.[1] These assumptions have called forth merited criticism from Prof. Richardson, of this city, and from Prof. Leeds, of Hoboken, both of whom emphasized the fact, singularly ignored by Cutter, Jacobi, and their followers, that ordinary white wheat-flour contains a varying but always notable quantity of gluten.

So far as the writer is informed, however, there has not been recorded any ocular demonstration of the gluten of the wheat-grain, *in situ* and entirely independent of the "gluten-cells." Such a demonstration may be conclusively made by either of the following methods:

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[1] E. Cutter, M.D., Galliard's Med. Jour., Jan. 1882.

1. If whole wheat-grains be macerated in water to which a few drops of ether have been added to prevent germination, they will, in a few days, became thoroughly softened, and the contents of each grain may then be squeezed out as a white tenacious mass. Examination of the remaining bran shows the "gluten-cells" undisturbed, closely adhering to the cortical protective layers. By now carefully washing the white extruded mass, the major part of its starch may be removed; and upon the addition of a drop of iodine solution, microscopic examination shows numerous net-works of fine yellow fibrils, still holding entangled in their meshes many starch-granules colored blue by the iodine. In carefully-washed specimens, these sponge-like net-works are seen to retain the outline of the central starch-filled cells, and evidently constitute the protoplasmic matrix in which the starch-granules lay. Upon gently teasing such a specimen under a moderate amplification the fibrils will be seen to become longer and thinner in a manner possible only to viscid and tenacious substances,—a class represented in wheat by gluten alone.

An eminently satisfactory proof of the proteid nature of these central net-works may be obtained by heating the specimen in the solution of acid nitrate

of mercury (Millon's reagent), when the fibrils will assume the bright pink tint characteristic of albuminoids under this treatment. The results of the application of the xanthoproteic and biuret reactions are equally conclusive, but more care is required in the use of these proteid tests, and the resultant differentiation is not so clear. Reticuli similar to those above described, but much broken and smaller, may be seen, upon close examination, scattered throughout fine white flour, without the addition of any reagent.

By general consent, the albuminoids of the wheat-grain are grouped together as gluten, which is, however, further separable into gluten-fibrin, gliadin, and mucedin, proteid bodies practically equal in nutritive value, but differing in certain physical properties, notably that of solubility. It must, therefore, be borne in mind that in this, as in all other methods of separating gluten from the other constituents of the grain, its relatively small soluble portion is removed with the starch, and that any estimate of the quantity of gluten based upon such methods will probably be rather under than over the actual amount.

2. In even the thinnest sections of the wheat-grain, the gluten of the central portion is always masked

by large numbers of starch-granules. These may, to a large extent, be removed by immersing the section for a short time in liquor potassæ, with subsequent careful washing. The alkali effects the hydration and partial solution of the starch; but if its application be too long continued, the gluten will also be dissolved. This treatment is well adapted to show the rather dense gluten net-works usually found in bran, immediately below the fourth layer.

3. The most satisfactory method of studying the distribution of gluten in sections of wheat is that of *artificial salivary digestion.* If the section be gently boiled for a moment to hydrate the starch, then transferred when cool to filtered saliva, and maintained for from half an hour to an hour at a temperature of about 98° Fahr., all the starch will be digested away, while the insoluble proteid and other constituents will remain entirely unaltered. A section of wheat-grain thus treated will exhibit, throughout its entire central portion, close-meshed gluten net-works, which become slightly denser toward the cortex of the grain. The proteid character of these reticuli is here, as in the first method, susceptible of micro-chemical demonstration by Millon's reagent or the biuret reaction. A relatively very faint coloration, indicating the presence of

albuminoids, is noticeable in the "gluten-cells," while the gradual condensation of the gluten of the endosperm as the cortex is approached, is evidenced by a quite vivid coloration of the fibrils.

Schenk[1] has applied Millon's reagent to sections of wheat with a resultant assumption by the endosperm of a pink tint and "no coloration of the cortical gluten-cells." The starch was not removed, and the method of distribution of gluten was not determined. By artificial gastric digestion of wheat sections, the same observer noted that the starch of the section became readily detached, and deduced from this the just proposition that the gluten lay between the starch-granules.

Objections are not infrequently offered by the chemist to the microscopical determination of organic compounds, especially where any attempt at a quantitative estimation is made. All that is claimed for the methods above described is the demonstration of gluten in very considerable quantity in the inner layers of the wheat-grain. It is but just to state, however, that by these methods a conception may be obtained of the quantity of proteids within the grain fully as accurate as that given by the usual

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[1] Anat.-Physiol.-Unters., p. 32. Wien, 1872.

chemical method of estimating the albuminoids of a given body, namely, from the entire amount of nitrogen contained in it. Especially is this true in the case of vegetable tissues. In a close analysis of the potato, Schultze and Barbieri found that only 56.2 per cent. of all its nitrogen existed in albuminoid combination, while in the fodder-beet only 20 per cent. of the nitrogen went to the formation of albuminous compounds; the remainder in each case entering into the composition of non-nutritious bodies, as amides, nitrates, ammonia, and asparagin.

The fact that the gluten net-works become denser toward the periphery of the endosperm, together with the presence of non-albuminoid nitrogenous compounds in the perisperm, explains the notable percentage of nitrogen found in bran as ordinarily roughly removed.

The color-tests mentioned above indicate that the amount of proteids contained in the cells of the fourth layer is relatively very slight; but admitting for the moment that these cells contain gluten, the question naturally arises whether, in view of their dense cellulose walls, they are capable of serving as a food-stuff for man. In artificial digestion the writer has found these elements, even when thoroughly cooked, to be unaffected by the digestive

juices; that is, well-boiled bran with its adherent "gluten-cells," will sustain prolonged maceration at the temperature of the human digestive tract in artificial gastric and pancreatic juice (in which, under the same conditions, fibrin is readily digested) without exhibiting any change. These cells were further found to be unaffected by maceration for thirty days in liquor potassæ, except for a slight swelling of the cell and the occasional coalescence of some of its contained oil-globules. They were also practically unchanged by a few days' immersion in strong nitric acid. In order to obtain conclusive and unassailable results as to the nutritive value of the "gluten-cells" as far as man is concerned, the writer has at present under observation a number of healthy adults, who daily receive, in addition to their regular diet, a small fixed amount of boiled bran. Their alvine dejections (containing all the undigested elements of food after the normal action of all the digestive juices) will be submitted to close microscopical examination, with a view to ascertaining the extent to which the "gluten-cells" have been digested, and a report will be made upon the results in the near future.

IV.

ON CERTAIN UNTOWARD EFFECTS OF THE ADMINISTRATION OF TURPETH MINERAL.

We have recently had under our personal observation five cases in which the administration of turpeth mineral was followed by unexpected symptoms.

On the occasion in question each of eight well-nourished men, in average health, was given five grains of turpeth mineral;[1] and as emesis did not follow within half an hour, three grains additional were given, with the result of inducing vomiting, more or less copious, within twenty minutes after the administration of the second dose. Beyond a continuation of the retching for some time and a general complaint of a sense of burning in the throat and fauces, nothing unusual was observed at the time, and but little depression immediately followed the emesis.

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[1] The drug was purchased from a reliable wholesale dealer in this city.

On the following morning, however, our attention was called to the condition of five out of the eight men above mentioned. A rather violent diarrhœa had followed in from ten to twenty hours after the administration of the drug, attended by much griping and a rather unusual amount of constitutional depression. Each of these five men had passed in the twenty-four hours succeeding the exhibition of the drug from eight to fifteen stools. These stools at first resembled those of calomel, but eventually became yellow. Appropriate treatment was administered, and on the following day the diarrhœa was partially or wholly checked, and the cases progressed favorably to recovery. It is worthy of note that in each case the first few stools contained minute particles of the yellow sulphate, showing that not only had its elimination by emesis been far from complete, but also that the drug had been for from ten to twenty hours in contact with the tissues and fluids of the digestive tract.

In the fifth case, John H., a German, æt. 38, complained of a soreness of his gums, and of the large amount of saliva dribbling from his mouth. He had up to this time received no preparation of mercury for several months. An examination showed the gums to be soft and spongy, with the

teeth partially loosened, the tongue swollen, covered with a thick, yellowish coat, and showing distinctly the imprint of each tooth. This, together with the large amount of saliva secreted, and the characteristic fetor of the breath, proved it to be a well-marked case of salivation, such as is fortunately rarely witnessed at the present day, either in hospital or general practice. Under appropriate treatment, however, the man improved, and was ultimately cured.

Had the cases been younger or less vigorous, a different termination might have resulted.

At the time we regarded these results as peculiar, but shortly afterwards our attention was called to an article by Dr. McPhedran,[1] in which was given a detailed account of two fatal cases occurring in children, in which, however, emesis failed to result, as also a similar case in the *Medical and Surgical Reporter*.[2]

Upon examining the literature of the subject we find that Dr. Hubbard, of Maine, was among the first to use this drug; but to Dr. Fordyce Barker, of New York, belongs the credit of bringing it

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[1] The Medical News, December 22, 1883, p. 682.

[2] January 19, 1884, p. 93.

prominently before the attention of the profession. In an article on "Croup,"[1] Dr. Barker states that after an experience of twenty years he considers turpeth mineral the best emetic for use in this disease, and goes so far as to recommend that it be kept on hand in all families with children of a croupy tendency, administered at the earliest symptoms of an attack, and before sending for a physician.

Abroad, also, the drug seems to have been received with favor. Drs. Desmartis and de Titray,[2] who consider the membrane in croup as due to the result of blood-poisoning of a fermentative character, advocate the merits of the remedy as twofold, viz., as exerting a specific agency upon the ferment, and also as removing the deposits by emesis. They record its use in a number of cases of different ages with good results.

Again, Dr. Smith,[3] in his work on "Diseases of Children," speaks of this drug in connection with croup, and mentions it as probably the best emetic in ordinary cases of this disease.

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[1] American Journal of Obstetrics, May, 1870.

[2] Nouveau Traitement du Croup, etc., Paris, 1860, p. 28.

[3] Fifth edition, p. 548.

Prof. Alfred Stillé[1] quotes two cases occurring in adults with fatal results. In one, a boy, aged sixteen, took about a drachm of this drug; symptoms of the ingestion of an irritant poison followed, together with great salivation, and death ensued in a week's time.[2]

"In the second case, a man, æt. 27, took forty grains of this medicine by mistake for Æthiops mineral. The primary symptoms were precisely the same as in the above case just related. Death occurred at the end of ten days. The inner surface of the mouth, gums, palate, and fauces were covered with black sloughs; the parotid and submaxillary glands were enlarged; the mucous membrane throughout the intestinal canal was softened and easily torn; the glands of the stomach and intestines unnaturally large; the kidneys were much enlarged, and the bladder full of urine."[3]

A case of poisoning, with recovery, by the same drug, in a dose of "less than a drachm," is reported by Yowndes.[4]

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[1] Therapeutics, fourth edition, vol. ii. p. 769.

[2] Letheby, London Medical Gazette, xxxix. p. 474.

[3] Taylor, Guy's Hospital Reports, 3d series, x. 180.

[4] Abstract in Lancet, March 10, 1860.

In the "United States Dispensatory"[1] we find it stated that the drug in question operates with great promptitude, but sometimes excites salivation.

As seen by the references above given, our cases present little of novelty, excepting that the dose we used was quite within therapeutic limits as ordinarily given; but we deem it our duty to call attention to the danger attending the administration of this drug, especially as its poisonous properties seem to have been overlooked by several recent writers on therapeutics.

Prof. Bartholow,[2] it is true, states that "serious results might be produced if emesis did not so promptly follow," which seems to agree with the experience of Dr. McPhedran, already mentioned. In the cases under our own observation, however, the poisonous symptoms followed, notwithstanding that fairly copious emesis resulted in every case. The time which elapsed between exhibition and emesis (thirty-five to fifty minutes) was possibly sufficient to permit the occurrence of chemical changes in the drug as it lay in the stomach, and

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[1] Fifteenth edition, p. 767.

[2] Therapeutics, fifth edition, p. 252.

the minimum time of ten hours elapsing between the ingestion of the drug and its final elimination with the fæces was (in one case at least) fully sufficient to account for the resultant symptoms, which were of a character tending to substantiate the statement of Miahle, that all mercurial preparations are absorbed in the form of chlorides.[1]

We are informed by several prominent dealers in drugs that the demand for turpeth mineral is quite large, and is apparently growing. This fact, together with the praise it has received in several quarters, justifies us in emphasizing the following conclusions, based upon the observations, old and new, which are given above:

1. That a dangerous quantity of turpeth mineral often remains in the stomach after emesis.

2. That this drug possesses sufficient toxic and irritant properties not only to demand from the profession much more than usual caution in its administration, but to condemn its use where the exhibition of any other emetic is practicable.

3. That it should not be placed in the hands of the laity.

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[1] See the Medical News, January 26, 1884, p. 89.

V.

A PRELIMINARY NOTE ON A REACTION COMMON TO PEPTONE AND BILE-SALTS.

If the acid nitrate of mercury (Millon's reagent) be added to a cold aqueous solution of potassium iodide, a *red* precipitate of mercuric iodide always appears. When, however, either peptone or biliary salts are present in noteworthy amount, the precipitate of nascent mercuric iodide assumes the *yellow* phase. As practically applied, the red may vary from salmon to scarlet, the yellow from pale lemon to orange.

In order to render the test sensitive to the presence of minute quantities of the substances in question, it is necessary to limit the amount of potassium iodide employed. Thus to each five cubic centimetres of the suspected fluid—which must be cold and either neutral or faintly acid—are added two drops of a saturated solution of potassium iodide, the two liquids being well mixed.

Four or five drops of Millon's reagent are now added, the contents of the vessel thoroughly stirred or shaken. Under these circumstances the presence of peptone in amounts of less than one part in five thousand is readily shown. By reducing the quantities of the reagents used it is possible to demonstrate the presence of peptone in a solution containing but one part of that body in seventeen thousand parts of water.

The conditions interfering with this reaction are: alkalinity of the fluid examined (readily overcome by neutralization); heat, which has the same influence upon the nascent mercuric iodide as have peptone and the bile-salts; and the presence of certain compounds, as potassium ferrocyanide, which chemically prevent the production of the mercuric iodide.

The following bodies in moderate amount do not affect the reaction: saliva, syntonin, amygdalin, para-albumen, diastase, kreatin, leucin, tyrosin, mucic acid, glucose, urea, uric acid, nitric, hydrochloric, sulphuric, and picric acids, glycerine, alcohol, atropia sulphate, pilocarpin nitrate, caffeine, sodium carbonate, ammonium oxalate, sodium phosphate, and manganese chloride and ferric chloride.

[This test is not applicable to urine, nor is it available in the presence of albumen or gelatin.]

It is obvious that this reaction is useless to the student as an isolated test, inasmuch as it responds to two entirely distinct compounds, but its simplicity and striking colorations give it very considerable value when employed in corroboration of other tests.

VI.

A NOTE ON THE BEHAVIOR OF HYDROBROMIC ACID AND OF POTASSIUM IODIDE IN THE DIGESTIVE TRACT.[1]

I VENTURE to present before the Society a brief note upon a subject not strictly neurological, but having direct bearing upon the relations entertained to the processes of digestion by two drugs, which are of interest to the neurologist.

In a series of artificial digestions, in which hydrobromic acid was present in the digestive mixture in amount corresponding to the therapeutic dose, I have noted,—

(*a*) That salivary digestion was completely suspended, whereas

(*b*) The peptonization of proteid food-stuffs was

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[1] The general deductions herein made from the study of these two drugs are applicable respectively to all acid and alkaline drugs given by the mouth, and a more descriptive title of the paper would have been "Time Relations in the Exhibition of Acids and of Alkalies."

in no wise retarded, the variation from the normal, if any, being toward an acceleration of this process.

It is evident, therefore, that, other things being equal, the appropriate time for the exhibition of this drug is immediately upon the cessation of salivary digestion within the stomach, or, in other words, upon the first formation of free acid within that viscus.

Recent studies[1] have shown that the acidity of the gastric contents, found even in quite early stages of digestion, is not due to the presence of *free* acid; and the ingenious observations of Von den Velden[2] go far toward proving that the development of free acid within the stomach does not occur until from forty-five minutes to an hour after breakfast, and from one to two hours after dinner. These results were obtained chiefly by the use of methyanilin violet and tropæolin, bodies delicately responsive, by color-change, to the presence of free acid. There is little doubt in my mind that hydrochloric acid is developed in the stomach at an earlier period than that

[1] Deutsch. Archiv Klin. Med., xxiii. 369. See also Jahresb. ü. d. Fortschr. d. Thier-Chemie, 1880, p. 302, and Danilewsky, Centralb. f. d. Med. Wiss., 1880.

[2] Zeitschr. f. Physiol. Chemie, iii. 205.

above indicated, but it seems very probable that by immediate combination with albuminoids it loses somewhat of its characteristic activity. This is illustrated by an observation made in the course of this study, namely, that the addition of small amounts of potassium iodide to dilute solutions of acid-albumen containing two-tenths of one per cent. of hydrochloric acid does not result in the liberation of iodine. The addition of the same amount of the iodide to the same quantity of an aqueous solution of hydrochloric acid of the same degree of acidity results in an immediate liberation of iodine.

This interesting discovery of two stages of acidity in the gastric juice has, I believe, not yet been incorporated in the text-books. It serves to reconcile the contradictory opinions so frequently found as to the value to the economy of saliva as a digestive fluid, and explains the completely diverse results obtained by such careful workers as Frerichs,[1] and Bidder, and Schmidt.[2]

Besides an observance of the time-limitations just indicated, I would suggest the advisability of milk

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[1] Wagner, Handwoerterbuch d. Physiologie, iii., a, 772.

[2] Bidder und Schmidt, Verdauung u. Stoffwechsel, p. 27.

as a vehicle for the administration of hydrobromic acid. The curd thus formed is fine and flocculent, the mixture closely resembling buttermilk in taste and appearance, and in no wise suggesting medicine. I have taken as much as a tablespoonful of the dilute acid in a tumbler of milk without any repugnance. The milk used must be raw. With this, as with most other acids, boiled milk gives tough and bulky coagula.[1]

As regards the exhibition of the iodide of potassium, the *rationale* of its time relations is altogether different. Although this drug is distinctly alkaline, its presence in a mixture of hydrated starch and saliva certainly does not suspend the action of the amylolytic ferment, nor, so far as I can determine, materially retard it.[2] When, however, the iodide is added, even in very small amount, to a mixture of artificial gastric juice and egg albumen or fibrin, the rapidity of peptone formation, as determined by the

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[1] Randolph: Verbal Communication on Differences between Raw and Boiled Milk.—*Proc. Acad. Nat. Sci. of Phila.*, 1884, p. 120.

[2] Langley & Eves, Jour. of Physiology, iv., p. 19, have shown that although a distinctly alkaline medium retards salivary action, the presence of a proteid body in the digestive mixture will prevent this retardation.

nascent mercuric iodide reaction[1] or by the biuret reaction and control test, is greatly diminished. This result is not due to a slight diminution in the acidity of the solution, caused by the addition of an alkaline body; for the same effect is noted when the acidity of the solution is at once again brought up to the normal degree. The pepsin is apparently but little, if at all, affected by the presence of the iodide, if we may judge by the indifference of ptyalin to the drug, and by the fact that quantities of the iodide corresponding to the maximal therapeutic dose neither entirely suspend the peptic activity, nor induce greater retardation of the digestion than do much smaller quantities. A slight effect is exerted by the iodide upon the proteid food-stuffs, evidenced in an increased toughness produced in, *e.g.*, fibrin, and, when the drug is abundantly present, in the acquisition by the albuminoid of a slightly yellow tinge, due to staining by iodine, which is liberated by the free acid of the artificial gastric juice.

The most important factor in the delay of peptonization lies in the power possessed by potassium

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[1] Randolph: A Reaction Common to Peptone and Bile-salts.—*Proc. Acad. Nat. Sci. of Phila.*, 1884.

iodide, even in relatively minute quantity, of precipitating acid albumen in solutions, which shall, after its addition, possess the normal degree of acidity of human or even canine gastric juice. The same may be said of potassium bromide and of several other analogous compounds. The precipitation effected by the iodide is so complete that when solutions of acid-albumen are thus treated and filtered, the still acid filtrate yields no trace of proteid matter. This observation, which is doubtless old, though I have been as yet unable to find it recorded, tends to show that the time at which the administration of this drug is least liable to disturb digestion is either during or immediately after the ingestion of food.

There are several sources of error in attempts at deduction from the results of artificial digestion, as ordinarily performed. Thus the continued activity of a digestive fluid is largely conditioned by the removal of the products of its action soon after their formation. This occurs in the living viscus, but not in the test-tube of the experimenter. The maintenance of the normal temperature of the active stomach is, of course, readily accomplished, but the conscientious imitation of other factors in the normal digestive process implies not only a constant

mechanical intermingling of food-stuff and digestive fluid, but the continued addition of small amounts of the digestive fluid itself. I have nearly perfected an apparatus which in a large degree obviates the difficulties just cited.

In it artificial salivary digestions are conducted in a thin tube of fish-bladder, closed at one end, which is, by mechanical means, kept in gentle agitation. The contents of this tube are maintained at the proper temperature by a surrounding body of warm water which is slowly but constantly changed. For gastric digestions the animal membrane is substituted by one offering equally great surface for dialysis, but resistant to peptic action. Despite, however, the inaccuracies attending existing methods of study, the following deductions from the facts, old and new, which are here presented, appear justifiable.

I. That the earliest production of free acid within the stomach is approximately three-fourths of an hour after a meal; its appearance being still futher delayed by the ingestion of food in large quantity.

II. That hydrobromic acid is liable to impede the digestion of starchy foods when administered with the interval just named; and,

III. That iodide of potassium should be given at such time and in such dilution that its absorption shall be complete before the appearance of free acid within the gastric contents.[1]

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[1] Since this paper was read, I find that Landois in the last edition of his "Lehrbuch der Physiologie," 1885, p. 306, accepts without question the results of Von den Velden and others here summarized. The same authority (p. 311) quotes Fubini and Fiori as stating that potassium iodide impedes gastric digestion. Chambers, in his "Manual of Diet," Philadelphia, 1875, p. 257, advises that potassium iodide be administered before meals, "as the mixture of the drug with food in the stomach diminishes the efficiency of both."

VII.

ON THE DIGESTION OF RAW AND OF BOILED MILK.

Dr. N. A. Randolph referred to certain profound changes produced in milk by boiling. In this operation the casein is not coagulated, but there is an evolution of sulphuretted hydrogen (Schreiner), a diminution in the gaseous constituents of the fluid and a change in the amount of ozone present.

The most striking difference between raw and boiled milk lay in their respective responses to rennet and acids.

At the body-temperature the firm coagulation of raw milk occurred almost immediately upon the addition of a neutral rennet solution, whereas boiled milk, under the same conditions, did not clot for a far longer period, and the coagula were not firm. On the other hand, dilute or strong acids were tenfold as active upon boiled as upon raw milk. Some time after making these experiments Dr. Randolph found that so far as acids and rennet were con-

cerned, similar results had been obtained by Schreiner (Chem. Centralbl., III. Folge, IX. Jahrg.), and he desired to present his observations in these particulars simply as confirmatory of those of that observer.

Artificial digestions showed that milk was more readily digested when raw than when boiled. This was further confirmed by a comparative examination and weighing (in over fifty cases, and in which he was aided by Dr. Roussel) of the contents of the stomach after raw and boiled milk had been, in different individuals, undergoing actual gastric digestion. In these cases the residue found in the stomachs of those persons receiving boiled milk was greater than the similar residue found in the stomachs where raw milk had been undergoing digestion for the same length of time. [In obtaining the gastric contents of the individuals under observation, turpeth mineral was used in the first series of eight persons with most unsatisfactory results. It was always thereafter substituted by hypodermic injections of apomorphia.]

VIII.

A STUDY OF THE NUTRITIVE VALUE OF BRANNY FOODS.

From an economic stand-point the question of the nutritive value of bran is one of great importance, for the removal of this portion of the wheat implies a loss of from 17 to 20 per cent. in the weight of the grain. In spite of this loss, which necessarily renders white bread more expensive than that made from whole wheat-flour, even the poorest inhabitants of most civilized countries where bread is not the staple food, insist upon eating the bread made from the finer grades of flour. A tendency so widespread as this would apparently indicate the unconscious summation of the experiences of many generations, and go far toward proving the propriety of such a selection.

The use of flour representing the entire wheat-grain has, however, been long and ably advocated; the reasons given for the retention of bran being that its removal entails the loss of,—

I. "Nutritive salts" (Nährsalze of Liebig).

II. Carbohydrates.

III. Proteids, notably gluten.

The facts, also, that branny foods in common with many others will spur an atonic bowel to activity, give due bulk to its contents, and induce the passage of stools of the normal or feculent consistency are noteworthy, but their further consideration is beyond the limits of the present paper. The other reasons for the retention of bran in wheat-flour will be discussed *seriatim*.

I. The fact that fine flour contains a much smaller percentage of salts than does either bran or the whole wheat—a fact evidenced by the relatively small amount of ash which it yields—forms the basis of the theory of Liebig,[1] that in the removal of bran nutritive salts of value are lost. The investigations of Meyer[2] and Forster[3] are often cited as showing that after the removal of bran, these salts are still present in quantity sufficient for the needs of the economy.

Our experiments upon young pigs, described further on, show that although survival is quite pos-

[1] Chemische Briefe, 1851.

[2] Zeitschrift f. Biologie, vol. vii. p. 33.

[3] Ibid., vol. ix. pp. 293–380.

sible upon an exclusive diet of bread from white flour, growth is much more active upon a diet of bread containing a greater amount of inorganic matter. It is possible that Liebig's estimate of the needful amount of inorganic matters was too high, but it is equally noteworthy that there is a tendency on the part of late writers to give insufficient prominence to the importance of these elements of food. It may not be out of place here to mention a striking illustration of the absolute necessity for inorganic salts in the fluids of the economy, as recorded by Dr. S. Ringer.[1] This observer found that while minnows were kept in ordinary tap water they would live for weeks unfed. When, however, they were placed in distilled water they died on an average in four hours and a half. Further, that in a rude imitation of spring water, made by the addition to distilled water of potassium and calcium chlorides, and of sodium bicarbonate, the fish lived on an average about two weeks. Study of the factors in the experiments showed that death was due to a diminution of salts in the economy of the fish. That such diminution, even when very slight, could

[1] Journal of Physiology, vol. iv. No. vi., Feb. 1884, in the appended Proc. Physiol. Soc., session Dec. 13, 1883.

result fatally, was shown by an analysis of the distilled water after the death of the fish; traces only of inorganic matter being found.

II. The loss of carbohydrates involved in the removal of bran, appears at first sight not inconsiderable, as it amounts to about 20 per cent. of the carbohydrates present in the entire grain. The members of this group represented in bran are starch and cellulose. The former is present in extremely small amount, while the latter, as has been proven by the experiments of Donders,[1] Mulder,[2] and Poggiale,[3] is digestible in any noteworthy degree[4] by the herbivora only. The observer last named subjected a given weight of dry bran to the successive actual digestions of two dogs and one hen, and, thereafter, was able to recover over 65 per cent. of its non-nitrogenous constituents. The loss in cellulose was probably much less than that here indicated, for we have found that during the maceration of bran in the digestive tract, certain portions

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[1] Nederl, Lancet, vol. vi. pp. 227, 244.

[2] Physiologische Chemie, p. 1024.

[3] Comptes-Rendus, vol. xxxvii. p. 173.

[4] See, also, Weiske (Centralblatt, No. 26, 1870), who finds that a small percentage of cellulose, especially when cooked, is dissolved in the human digestive tract.

become detached from the main flake, and are with the greatest difficulty recovered.

III. Wheat-bran contains a considerable but varying proportion of nitrogenous compounds, averaging, however, about 14 per cent.[1] This fact has permitted the continued existence of two widely credited assumptions: (*a*) That this nitrogen exists in albuminoid combination, or, in other words, is in a nutritious form; and (*b*) that the proteïd matter of wheat is contained almost exclusively in specific cortical cells of the grain,—the so-called "gluten-cells."

(*a*) Nearly all the existing estimates of the proportion of proteids in food-stuffs are based upon the hypothesis that all of the contained nitrogen is present in some albuminoid combination. The percentage of nitrogen in a given food is therefore ascertained, multiplied usually by either 6.5 (Payen) or 6.33 (Ritthausen) and the result recorded as the percentage of proteid matter. It has lately been

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[1] Dempwolf, Ann. d. Chem. u. Pharm., vol. cxl. p. 343. His figures, of interest here, are as follows: The amount of nitrogenous matter in the whole wheat was 14 35 per cent. The amount varied in the different grades of white flour from 11.01 to 15.56 per cent. The nitrogenous matter of the two grades of bran made from this wheat was respectively 13.93 and 14.06 per cent.

conclusively proven that nitrogen in non-albuminoid combination—*i.e.*, in compounds not capable of affording nourishment to any of the higher organisms—is present in many food-stuffs, and especially in those of vegetable origin. As a case in point may be mentioned the analysis of Wigner,[1] in which it is shown that of the total nitrogenous matter of the entire wheat-grain, 87.9 per cent. is coagulable,—*i.e.*, distinctively proteid. Of the bran only 42.4 per cent. of its nitrogenous compounds are coagulable, whereas, in the flour, 89.7 per cent. of these bodies come under the head of true proteids. Yet more marked instances of the inaccuracies attending the ordinary methods of estimating proteids have become evident in the course of researches by Schulze and Barbieri,[2] who find that of the entire nitrogen of the potato but 56.2 per cent. enters into the composition of albuminoid matter, while in the fodder-beet only 20 per cent. of its contained nitrogen is thus combined, the remaining 80 per cent. aiding in the formation of amides, nitrates, and ammonia. It is evident from these facts that estimates of the nu-

[1] Der oesterr. ungar. Müller, 1879, p. 52.

[2] Quoted by Voit, Hermann's Hdb. d. Physiol., vol. vi. p. 462.

tritive value of branny and other foods, based upon the percentage of nitrogen present, must be received with caution.

(*b*) The term "gluten-cell" is, through a widespread misapprehension, applied to the cells constituting the fourth layer (Parkes) of the wheat-grain. These cellular elements exist usually in a single stratum, as irregularly cuboidal bodies in each of which, surrounded by a dense and laminated cellulose wall, is seen the semi-opaque granular contents. Upon the addition of reagents, especially in the form of caustic alkaline solutions, there is almost constantly noticeable a differentiation of the contents strongly suggesting the presence of a nucleus. Under these conditions, also, a coalescence of many of the individual granules forming the contents occurs with the formation of several highly refractive spheroidal bodies, an appearance which has led Payen (as quoted by Dr. Richardson) to use the name oléifères as a synonyme for the cellular constituents of the fourth coat. The hypothesis that the cells of this layer are the chief gluten-bearers of the wheat-grain is usually attributed to Donders.[1] The

[1] Nederl, Lancet, iv. 739; vi. 227, 244. Third series, vol i. 377.

return of bran to flour was at about the same period also advocated by Millon and Mége Mouriès.[1]

From this time on, with but few dissenting voices, the "gluten-cell" has been generally spoken of as the index of the nutritive nitrogenous matter[2] of the

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[1] Comptes-Rendus, vol. xliv. p. 47.

[2] By general consent the albuminoids of the wheat-grain are grouped together as gluten, which is, however, further separable into gluten-fibrin, gluten-casein, gliadin, and mucedin, proteid bodies practically equal in nutritive value, but differing in certain physical properties, notably that of solubility. It must therefore be borne in mind that in all methods of separating gluten from the other constituents of the grain, its (relatively small) soluble portion is removed with the starch, and that any estimate of the quantity of gluten based upon such methods will probably be below rather than above the actual amount. Ritthausen (Die Eiweiss-Körper der Getreidearten, 1872) believes that a certain amount of true albumen should be included with the constituents of gluten just mentioned. An observation of Denis (Mémoire sur le sang, 1859) confirmed by Hoppe-Seyler (Med. Chem. Unters., 1867) and Weyl (Ber. d. deutsch. Chem. Ges., xiii. 10, 1880) demonstrates that a portion of the proteids of the cereals exists in the form of a globulin. Thus the observer last named has shown that in wheat-flour treated with a 15 per cent. solution of sodium chloride, no formation of gluten occurs. We have found that bran, when macerated in 15 per cent. salt solution, yields a considerable amount of proteid matter precipitable by nitric and picric acids. We incline

wheat grain, while the central portion included within this layer, and constituting fully 80 per cent. of the grain, has been popularly regarded as being made up almost exclusively of cellulose and starch, and attempts have even been made to estimate the nutritive value of certain cereal food-stuffs by a microscopical determination of the proportion of "gluten-cells" present.[1]

The manifest impropriety of such methods has of late been strongly emphasized by Prof. Richardson, of this city, and Prof. Leeds, of Hoboken. The credit of the first disproof of the exclusive limitation of gluten to the cells of the fourth layer is probably due to Schenk,[2] who treated sections of wheat-grain with Millon's reagent, a pink coloration of the endosperm resulting. This coloration was most vivid at the periphery, indicating a gradual condensation of the proteid constituents of the grain as the cortex was approached. The same writer found "no coloration of the 'gluten-cells' as a result of this reagent," an observation which we cannot confirm; for, apart from the readily demon-

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to believe, however, that this is not a true albumen. (See Vines, Journal of Physiology, vol. iii. p. 93.)

[1] E. Cutter, M.D , Gaillard's Med. Journ., Jan. 1882.

[2] Anat.-Physiol. Untersuch., p. 32, Wien, 1872.

strable slight coloration of the contents of "gluten-cells" after the application of Millon's reagent, it is more than difficult to conceive a cell, however specialized, which shall exhibit no proteid matter as a portion of its contents. Schenk also noted in artificial gastric digestions of sections of wheat, that the starch-granules which (to a great extent) fill the cells of the central portion of the grain became detached, and from this fact deduced the just proposition that the starch-granules lay imbedded in some albuminoid substance. In a study of the distribution of gluten within the wheat-grain,[1] the senior writer has described several methods for the ocular demonstration of gluten, in very considerable amount, in that portion of the grain included within the fourth layer, and entirely independent of the "gluten-cells." The methods were as follows:

If whole wheat-grains be macerated in water, to which a few drops of ether have been added to prevent germination, they will in a few days become thoroughly softened, and the contents of each grain may then be squeezed out as a white, tenacious mass.

Examination of the remaining bran shows the

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[1] Randolph, Proc. Acad. Nat. Sci., Philadelphia, Dec. 11, 1883, p. 308.

"gluten-cells" undisturbed, closely adhering to the cortical protective layers.

By now carefully washing the white extruded mass, the major part of the starch may be removed; and, upon the addition of a drop of iodine solution, microscopic examination shows numerous net-works of fine yellow fibrils, still holding entangled in their meshes many starch-granules, colored blue by the iodine.

In carefully washed specimens, the sponge-like net-works are seen to retain the outline of the central starch-filled cells, and evidently constitute the protoplasmic matrix in which the starch-granules lay. Upon gently teasing such a specimen under a moderate amplification, the fibrils will be seen to become longer and thinner in a manner possible only to viscid and tenacious substances,—a class represented in wheat by gluten alone.

An eminently satisfactory proof of the proteid nature of these central net-works may be obtained by heating the specimen in the solution of acid nitrate of mercury (Millon's reagent), when the fibrils will assume the bright pink tint characteristic of albuminoids under this treatment. The results of the application of the xanthoproteic and biuret reactions are equally conclusive, but more care is

required in the use of these proteid tests, and the resultant differentiation is not so clear. Reticuli, similar to those above described, but much broken and consequently far smaller, may be seen upon close examination scattered through fine white flour, without the use of any reagent.

In even the thinnest sections of the wheat-grain, the gluten of the central portion is always masked by large numbers of starch-granules. These may to a large extent be removed by immersing the section for a short time in liquor potassæ, with subsequent careful washing. The alkali effects the hydration and partial solution of the starch; but if its application be too long continued, the gluten will also be dissolved. This treatment is well adapted to show the rather dense gluten net-works usually found adherent to bran immediately below the fourth layer.

The most satisfactory method of studying the distribution of gluten in sections of wheat is that of artificial salivary digestion. If the section be gently boiled for a moment to hydrate, the starch then transferred when cool to filtered saliva, and maintained for from half an hour to an hour at a temperature of about 98° Fahr., all the starch will be dissolved, while the insoluble proteid and other

constituents will remain *in situ* and entirely unaltered. The same result may be obtained from a somewhat more prolonged digestion of the unboiled section. A section of wheat-grain thus treated will exhibit throughout its entire central portion close-meshed gluten net-works, which become slightly denser toward the cortex of the grain. The proteid character of these reticuli is here, as in the first method, susceptible of micro-chemical demonstration. Upon the application of Millon's reagent to such a section, a relatively very faint coloration, indicating the presence of albuminoids, is noticeable in the "gluten-cells," while the gradual condensation of the gluten of the endosperm, as the fourth layer is approached, is evident even to the unaided eye.

The fact that the gluten net-works become denser toward the periphery of the endosperm, together with the presence of non-albuminoid nitrogenous compounds in the perisperm, explains the notable percentage of nitrogen found in bran as ordinarily roughly removed.

The small proportion of albuminoids present in the cells of the fourth layer as evidenced by their feeble response to the proteid tests, together with the very considerable quantity of gluten which we have shown to exist in the central four-fifths of the

grain (*i.e.*, the portion lying within the fourth layer), justifies us in the conclusion that by far the major portion of the nutritious nitrogenous matters exist in entire independence of the "gluten-cells."

The difficulties which attend the complete isolation of these cells, however, have as yet rendered impossible any accurate estimation of the proportion of their proteid contents. Admitting for the moment that the "gluten-cells" contain albuminoids in any noteworthy amount,[1] there are yet present conditions which seriously affect if they do not entirely nullify the nutritive efficiency of this portion of the grain.

The first of these conditions is the presence of the rough bran-scales, which, by increasing peristalsis, so hasten the passage of the entire intestinal contents that complete digestion and absorption are pre-

[1] Apart from the statement of Schenk, above cited, the entire absence of gluten in the cells of the fourth layer has been latterly affirmed by Mége Mouriès, who is quoted by Payen (Substances Alimentaires) to the effect that these cells are "filled with nitrogenous substances, of which gluten is not at all one." He finds the cells in question to contain, in addition to the salts of magnesium, lime, and potash, a peculiar diastatic ferment, cerealin, whose function is the transformation of the starch of the grain into dextrine and glucose for the nourishment of the germinating seed.

vented. The second is that, owing to the dense cellulose walls of the "gluten-cells," their contents are practically unaffected by the digestive juices. The fact that the presence of branny scales in the digestive tract prevents the thorough digestion of the intestinal contents, and induces the passage of fæces containing a considerable excess of undigested nitrogenous matter, is fully attested by the observations of Meyer and Rubner.[1] Edward Smith[2] has also closely studied the economic phase of this subject, and reports most unfavorably upon the use of branny foods, stating that the diminished absorption of nutritive matters, entailed by their use, more than counterbalances the (apparent) gain in cheapness. Of interest in this connection is the observation of Fr. Hofmann,[3] who noted that the amount of fæces passed upon a meat diet was remarkably increased by the addition of cellulose to the food taken.

The feeble response of the "gluten-cell" to reagents and digestive juices has been noted by several observers. Thus Donders[4] states that these bodies are digested by the herbivora, but not by dogs or

[1] Zeitschrift f. Biologie, vol. vii., ibid., xix. 1883, p. 46.

[2] "Foods," 1875, p. 175.

[3] Voit, Sitzgsber. d bayr. Acad., Dec. 1869.

[4] Physiologie (German ed.), p. 273.

man. Similar results are recorded by Poggiale,[1] and for domestic fowls by Meissner and Flüge.[2] J. Lehmann[3] records the feeding of pigs for thirty-two days on bran which contained almost no flour, with a nearly negative gain in weight, although the bran contained 15.5 per cent. of nitrogenous matters.

The ability of herbivora to digest "gluten-cells" and similar bodies is probably due to the relatively powerful amylolytic ferments of their digestive fluids, for it has been demonstrated that pepsin is unable to traverse cellulose.[4] It has also been shown by one of us[5] that the cells of the fourth layer are, to all appearance, entirely unaffected by prolonged artificial digestions,—salivary, gastric, and pancreatic,—and further that their contents were but little changed, and their walls in nowise disintegrated by immersion for some days in strong acids and alkalies.

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[1] Comptes-Rendus, 1853.

[2] Zeitsch. f. rat. Med., vol. xxxi. p. 185, and vol. xxxvi. p. 184.

[3] Amtsbl. f. d. Handl. u. wer. d. Königr. Sachsen, 1868, No. 2.

[4] Hammersten, Jahresber. d. Thierchemie, vol. iii. p. 207.

[5] Randolph, Proc. Acad. Nat. Sciences, 1883, p. 311.

Lately, however, in the course of an admirable paper upon the nutritive relations of gluten, Rubner[1] has stated that, although branny foods increase the amount of nitrogen in the fæces, fully three-fourths of the nitrogenous matter of bran is digested. In the bran used there was present 4 per cent. of nitrogen, "equalling 25 per cent. albuminoids," while in the bran obtained from the fæces of the persons under observation only 0.9 per cent. of nitrogen was obtainable. We hesitate in criticising the results of so able an observer, but it seems to us that there were two sources of error in this portion of his investigation. In the digestion of bran the free, adherent gluten, which properly belongs to the more central layers, is, of course, readily dissolved, with a consequent reduction in the nitrogen of the bran. Apart from this, however, a loss in nitrogen is to be expected, from the diffusion of nitrogenous crystalloids. Further, the "gluten-cells" become so separated from the true bran, during their maceration in the intestinal contents, that it is nearly, if not quite, impossible to recover them.

In order to satisfy ourselves regarding the digestibility of the cells of the fourth coat, we have

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[1] Zeitsch. f. Biologie, vol. xix. 1883, p. 46.

subjected bran with its adherent "gluten-cells" to actual digestion by twelve well-nourished adults, six males and six females. These twelve persons were selected from a larger number by excluding all whose fæces exhibited under microscopic examination any inefficiency in the amylolytic and proteolytic digestive ferments as evidenced by the presence of starch or muscle fibre in more than a minimal amount. Sources of error arising from individual peculiarities having been eliminated by the number of persons under observation, and the best conditions for digestion having been obtained, these persons then received daily for three days, in addition to their regular food, one ounce of thoroughly boiled bran. Their fæces for the last two days of the treatment were submitted to close microscopical examination, with results so nearly uniform as not to require tabulation. In every case the number of "gluten-cells" present was more than sufficient to render a diagnosis of the food taken a matter of great ease. In two-thirds of the cases no evidences of disintegration of any of the cells could be found upon repeated examination of many fields from each specimen. In four cases a small proportion (less than 10 per cent.) of the numerous cells examined showed evidences of having been affected by the

digestive process, the cell contents having become lighter in color and less opaque. If, however, any true digestion of the cells had occurred, it is evident that many of these elements in different stages of disintegration would have been seen.

As a rule, we found that the several layers of the bran presented an appearance not of having been digested, but simply of having been subjected to prolonged maceration. Thus the three coats of the true bran while entirely unchanged were frequently found separated from each other. We had expected to find the fourth layer closely adherent to the third, as is the case in dry bran, but in the majority of specimens these two coats became separated, and occasionally large sheets of "gluten-cells," to all appearance perfectly normal, were seen. As a rule, however, that portion of the fæcal mass representing the meal at which bran was taken[1] was found to contain these thick-walled cells in nearly every field.

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[1] We did not find it needful to give with the bran any coloring matter to differentiate in the fæces the meal at which it was taken, as the scales of bran were always a sufficient index. When requisite, such differentiation may readily be obtained by the method of Cramer (Zeitschr. f. Physiol. Chem., vol. vi. p. 354), or that of Rubner (l. c.).

A study of the nutritive relations of a given food may be approached from three sides: First, from that of the exact chemical composition of the food, a knowledge absolutely essential to any scientific scheme of diet. Second, from that of the various excretions of the individual or animal upon the diet in question; and, third, from the more clinical stand-point of study of the effects exerted by a given diet upon the growth and nutritive processes of the organism under observation. After an examination of branny food in the light of the first two methods, we attempted its study by the third. To this end six young pigs of the same litter, and all in fair health, were weighed and placed under the same conditions in pairs in three separate bins. Those in the first bin daily received bread especially made from whole wheat-flour, in amount corresponding to one-fourth pound of dry bread each. To those in the second bin was given a corresponding amount of bread made from wheat whose three external coats only had been removed. The pigs in the third bin received the best white bread in amount corresponding to the standard above mentioned. A sufficient (fixed) quantity of water was given twice daily. The following table shows the weight of each pair at the beginning of the observation, and

at the end of respectively ten and thirty-two days thereafter:

Bin.	Age.	Food.	Joint weight March 6.	Joint weight March 16.	Joint gain 10 days.	Joint weight April 7.	Joint gain 32 days.
	Weeks.		*Lbs.*	*Lbs.*	*Lbs.*	*Lbs.*	*Lbs.*
I.	6	Bread from whole wheat.	24.5	29.0	4.5	33.25	8.75
II.	6	Brown bread from decorticated wheat.....	24.75	28.25	3.5	34.50	9 75
III.	6	White bread.....	25.25	27.25	2.0	33.0	7.75

Comparison of these weights exhibits curious and apparently contradictory results, viz., that during the first ten days the gain was greatest in the pigs fed upon whole wheat bread, whereas at the end of thirty-two days of such feeding the gain was most pronounced in the pigs fed upon bread made from wheat whose three outer coats had been removed. The cause of this variation in results is not far to seek. At the commencement of the experiments the animals were small, and the food given was in each case more than sufficient to replace the waste in both the tissues and circulatory fluids. Even the pair fed upon bread containing the innutritious and waste-inducing bran, digested and absorbed sufficient proteid matter to supply the needs of the tissues, and normal growth was also favored by the

presence of a bulky intestinal contents of a mechanically stimulating nature, and also by the nutritive salts which were present in this bread in larger amounts than in others. On the other hand, at the end of the thirty-two days the animals had notably increased in size; the food given was then barely sufficient for the needs of the economy, and any conditions impeding its complete digestion and absorption produced a notable effect upon the rate of growth of these young animals.

It must be borne in mind that these experiments relate only to the value of the different breads when taken alone to the exclusion of other foods. The experiments of Rubner before cited leave no doubt that a white bread contains more assimilable nutriment than does one made from the whole wheat, but this does not render it a desirable food-stuff for exclusive use. On the contrary, a weaned, but still quite young omnivorous mammal thrives better upon an exclusive diet of bran bread than on white, and, presumably, because the earthy and alkaline salts are present in greater abundance in the former, and, also, because the indigestible constituents tend to give to the intestinal contents that bulk and consistence which are essential to the hygiene of the digestive tract. But, as has been shown by Edward

Smith and others, the branny scales are needlessly irritating, and unduly hasten the passage of food[1] but partially digested and absorbed. The end which popular hygiene attempts to effect by the retention of bran in breadstuffs can be better attained by other means. Thus the nutritive salts of food so frequently lost in ordinary methods of preparation are readily restored by the concentration of the liquor in which meats and vegetables are cooked into a soup stock, as is practised in almost every French kitchen. Again, the various fresh green vegetables used as salads yield in abundance these inorganic food-stuffs, the presence of which we have seen is indispensable to normal tissue activity. A further advantage of these and other succulent vegetables lies in the fact that their cellulose, while efficient in giving proper bulk and consistence to the stools, is, as compared with bran-scales, soft and unirritating to the digestive tract.

From the facts, old and new, which have been

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[1] An observation worthy of mention in this connection is that of Rubner, who finds that while the presence of much woody fibre and harder cellulose in the intestinal contents induces the passage of stools containing an excess of undigested proteid foods, the absorption of fats under the same conditions is not materially affected.

presented, the following deductions appear to us justifiable:

I. The carbohydrates of bran are digested by man to but a slight degree.

II. The nutritive salts of the wheat-grain are contained chiefly in the bran, and, therefore, when bread is eaten to the exclusion of other foods, the kinds of bread which contain these elements are the more valuable. When, however, as is usually the case, bread is used as an adjunct to other foods which contain the inorganic nutritive elements, a white bread offers, weight for weight, more available food than does one containing bran.

III. That by far the major portion of the gluten of wheat exists in the central four-fifths of the grain, entirely independent of the cells of the fourth bran-layer (the so-called "gluten-cells"). Further, that the cells last named, even when thoroughly cooked, are little if at all affected by passage through the digestive tract of the healthy adult.

IV. That in an ordinary mixed diet the retention of bran in flour is a false economy, as its presence so quickens peristaltic action as to prevent the complete digestion and absorption not only of the proteids present in the branny food, but also of other food-stuffs ingested at the same time; and,

V. That inasmuch as in the bran of wheat as ordinarily roughly removed there is adherent a noteworthy amount of the true gluten of the endosperm, any process which in the production of wheaten flour should remove simply the three cortical protective layers of the grain would yield a flour at once cheaper and more nutritious than that ordinarily used.

IX.

A METASTATIC HEAT REGULATOR.

THE instrument about to be described is adapted to maintain a constant temperature within any water- or air-chamber heated by gas, the degree of temperature thus maintained being adjustable at will.

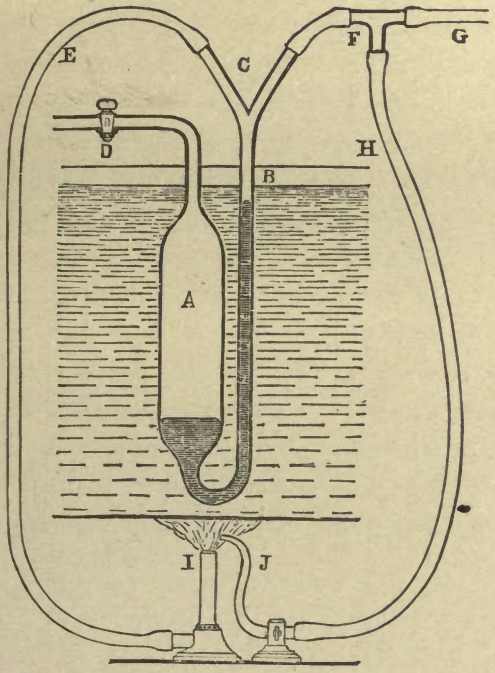
Reference to the illustration shows an air-thermometer so modified that the rise of mercury in the limb B will cut off the gas-supply which passes through its bifurcated extremity. A second modification lies in the accurately-fitting glass stop-cock D, connected with the air-chamber A. By means of this stop-cock the tension of the air within the chamber, and consequently the height of the mercury in the tube B, is readily adjustable. It is evident that when the mercury is forced high up in B, a relatively slight increase in the temperature of the surrounding medium will be sufficient to so expand the air in A as to force the column of mercury to the point of shut-off. On the other hand, a far higher temperature will be needed to effect the

shut-off when the columns of mercury in A and B are of the same height. In practice the adjustment is effected by placing the instrument in a medium of the required temperature, the cock D is opened, and air slowly forced in with a syringe, until the mercurial column in B is nearly at the point of bifurcation; the precise height varying, of course, with the dimensions of the instrument, and being readily ascertained by practice.

The pressure of the gas employed must be kept quite low, otherwise, as the mercury rises above the point of bifurcation, a portion will be blown out. One of the simpler gas-pressure regulators may be advantageously inserted between the source of gas-supply and the heat regulator. It is well also that the diameter of the limb C should be somewhat greater than that of its fellow, and also that its point of junction with B should be somewhat constricted in order that a smaller variation in temperature shall effect either the patency or occlusion of the gas exit.

When the mercury rises in B a trifle beyond the point of bifurcation, the passage of gas from G to E is arrested, and the flame from the burner I is at once extinguished. Were no further provision made, the vessel and its contents would soon cool

sufficiently to again permit the flow of gas, which would then pass off, unburnt, through I. This difficulty is obviated by the use of a second gas-jet, J,



so placed as to re-light the burner I, upon the renewed passage of gas, and so minute as not to give out sufficient heat to counterbalance that which is lost from the vessel by radiation, etc., during the

temporary stoppage in the main jet. This secondary jet may be readily made from a common brass blow-pipe, bent in the form shown in J, and steadily supported in such manner that its little flame may constantly play immediately above the opening of the main burner. It is usually necessary to still further reduce the small opening of the blow-pipe by squeezing it with pliers, or by other means. The secondary flame is fed by a branch, H, from the source of gas-supply.

The instrument must be protected from touching the base of the containing vessel either by suspension or by the intervention of a plate of cork or other non-conductor. It must also be held steadily vertical, and should always be accompanied by a thermometer to verify its adjustment. It is also well to have each of the exposed surfaces of mercury covered by a drop or two of glycerine to prevent oxidation.

X.

ON THE BEHAVIOR OF PETROLATUM IN THE DIGESTIVE TRACT.

THE mixture of hydrocarbons, recognized by the pharmacist under the name of petrolatum, and popularly used under the commercial names of cosmoline or vaseline, presents, on superficial inspection, few points of difference from some of the organic fats of the same consistency. Close examination reveals differences, both in physical properties and in chemical constitution, between the bodies just compared. One point of difference, which I have as yet been unable to find recorded, lies in the respective behavior of these two groups when in contact with the absorbent surfaces of the digestive tract. Thus, while the organic fats, as ordinarily taken in food, are readily and almost completely absorbed, this soft paraffine is entirely rejected, and found unchanged in the fæces.

During eight days I took, daily, one-half ounce

of commercial vaseline, in addition to my regular diet. Digestion was in nowise altered, and no appreciable results ensued. Later, two healthy adults each received, in the course of forty-eight hours, one ounce of vaseline. Their alvine dejections for three days from the beginning of this observation were collected and dried, and, at the suggestion of Dr. John Marshall, of the University of Pennsylvania, extracted with petroleum ether. Making a slight allowance for incompleteness in extraction, the vaseline ingested was, in each case, recovered in its totality, showing that it had passed through the economy unchanged and unabsorbed.

There are some important medical applications of these facts, the discussion of which would be out of place here, and which I reserve for further experiment;[1] but the following deductions appear permissible, and are of strictly biological interest:

I. Pure petrolatum, while entirely unirritating to the digestive tract, is valueless as a food-stuff.

II. The results of the experiments here described lend support to the theory that oleaginous matters

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[1] The chief medical use of these facts lies in the administration of vaseline as a bland emollient to the intestinal surface. I have in several individuals succeeded in checking diarrhœas of irritation by this simple means.

are dependent for their absorption, not upon mechanical, but upon vital activities, and that in such absorption the selective power of the protoplasm of the intestinal epithelium is manifested.

XI.

CUTANEOUS ABSORPTION OF NICOTINE.

Dr. N. A. Randolph described the results of a series of experiments performed by Mr. Samuel G. Dixon and himself, relative to the absorption of nicotine by the uninjured, healthy skin of the living rabbit. In these experiments only rabbits of ascertained good health were used. The fur of the abdomen was carefully clipped (not shaved); sufficient time, usually seven days, being allowed to intervene between this operation and the application of the drug to the skin, thus permitting any slight scratch made at this time to fully heal. The absence of cutaneous lesion was further confirmed by close examination under a strong hand-magnifier. The drug was then applied to the skin, no friction being used. In order to preclude the possibility of its vaporization and subsequent absorption by the lung-surface, the nicotine was placed upon an adhesive plaster, the backing of which was made of sheet-rubber. The plaster, with the drug in its centre,

was then applied in the open air, on a windy day. Different doses were applied; thus, in one case, one drop of nicotine, applied to the skin, caused death in five hours and eleven minutes. In each of three cases a similar application of ten drops was fatal in respectively one hundred and nine minutes, twenty-eight minutes, and thirty-six minutes. In the fifth case, a similar application of fifteen drops of nicotine caused death in twenty-eight minutes.

Of the ante-mortem symptoms, contraction of the pupil was *constant*, and often appeared very quickly. Other prominent symptoms were great trembling, with subsequent loss of muscular power in the extremities. In one case actual convulsions were noted, and in others, coldness of the skin and increased lachrymal and nasal secretion. Immediately upon the death of two of the animals (after the ten- and fifteen-drop doses respectively) blood was removed, defibrinated, and tested with mercuric chloride for the presence of nicotine in the manner detailed by Wormley (Micro-Chemistry of Poisons). In each of these two instances characteristic groups of crystals were found upon microscopic examination of the extract from the blood.

XII.

ON THE DIETETIC FACTOR IN THE TREATMENT OF ANGINA PECTORIS.

THERE has recently been under my care a patient suffering from true *angina*, in whom, as is not seldom the case, any slight gastric irritation constituted the immediate exciting cause of the frequently-recurrent paroxysms.

After the last attack there existed an inability to retain the lightest and simplest foods, their ingestion inducing not only nausea, but much cardiac distress. Recourse was had, with advantage, to milk, partially digested by the commercial Extractum Pancreatis; but the flavor of the resultant preparation was unappetizing, and finally became repulsive to the patient, who whimsically described its taste as that of "stewed corpse."

To meet this emergency, there were devised two food products, which I have not seen described, and which, in practice, proved eminently satisfactory.

1. *Pancreatized Oysters.*—The oysters of an or-

dinary stew (containing milk) are removed and finely minced, then returned to the liquid portion of the stew. The whole is brought to a temperature of 100° F., the appropriate proportions of pancreatic extract and sodium bicarbonate are added, and the mixture maintained at the temperature mentioned for thirty minutes, with occasional stirring. It is then strained and served, and forms not only a highly nutritious and palatable soup, but one which is retained by very irritable stomachs, and utilized with a minimum of digestive power. After boiling, to prevent the further action of the digestive ferment, gelatine may be added, and the mixture served cold as a jelly. Cooked tomato, onion, celery, or other flavoring suited to the individual taste of the patient, may be added at the beginning of the artificial digestion, and the solid residue removed in the final process of straining, at which time it will be noticed that the minced oysters originally added have been in great part dissolved.

2. *Pancreatized Milk-toast.*—Ordinary milk-toast, in which there is an abundance of milk, when digested in the manner just described, becomes an almost homogeneous pulpy mass, which, when the crusts have been removed, is usually acceptably retained by the irritable stomach. In extreme cases,

however, it may advantageously be strained and the fluid portion alone used, in which the partially peptonized solution of casein of the milk is reinforced by actually digested gluten and starch of the bread, together with a very little dextrin. Plain, light sponge-cake may be similarly digested, and occasionally forms a desirable change.

In conclusion, I would express the hope that these rather homely suggestions may prove of value in other hands, in extending the somewhat scanty bill of fare suited to patients suffering from gastric hyperæsthesia, and the various neurotic troubles of which such a condition may be the exciting cause.

XIII.

A PAINLESS ESCHAROTIC.

In view of the rapidly growing literature of cocaine it is not impossible that the application which we here briefly describe has already been employed; but, if so, it has escaped our scrutiny of the later developments regarding this drug.

When a saturated solution of cocaine hydrochlorate in strong nitric acid is applied to the uninjured skin, the ultimate result is precisely that which would occur upon the similar application of pure nitric acid, but the time required for the formation of a deep eschar is considerably longer in the former than in the latter case.

We have experimented with the mixture just mentioned upon several individuals, ourselves included, and can safely say that the sensations attending its application cannot be accurately described as painful. There is, however, a slight pricking sensation soon after the mixture is first dropped upon the skin.

Upon one person a control-experiment was instituted in the following manner: Upon his right arm were placed four drops of strong nitric acid, while upon the same point on his left arm was similarly disposed the same quantity of the mixture of nitric acid and cocaine hydrochlorate. The pure acid caused great pain, and was speedily removed; the mixture, which was applied later, caused a sensation described as "tickling, with slight pricking," which soon passed away.

In two cases the burned points were covered with absorbent cotton wet with a two per cent. solution of cocaine salicylate, a salt which we have not yet seen described, but which, in addition to the peculiar properties of its contained alkaloid, appears to be somewhat antiseptic. There has been no discomfort after the formation of the eschar. Prof. Harrison Allen, to whom we presented a portion of our solution of the salt last mentioned, kindly reports that he has applied it several times in his practice as a substitute for other salts of cocaine, with good results.

XIV.

A NOTE ON THE CUTANEOUS ABSORPTION OF SALICYLIC ACID.

In view of the fact that the internal administration of salicylic acid and its salts is not infrequently capable of producing or increasing gastric irritability, the advantages of inducing its cutaneous absorption are at once apparent. By the application to the uninjured skin of salicylic acid, rubbed up in a thin paste with olive oil, we have been able to demonstrate the presence of the drug in the urine in each of seven cases in which such application was made. In six of these cases, an existing rheumatic attack was relieved by the application. Of these, in one case only did the application give a negative result.

Case I.—Man, æt. 30, of rheumatic habit, who had been suffering for three days from rheumatic pains and stiffness in the right thigh. The pain had grown daily worse, until motion of the limb became

almost unbearable. He was ordered to remain in bed, and twenty grains of salicylic acid were rubbed into a paste with olive oil, and gently smeared in each axilla. Four hours thereafter, the patient felt somewhat better; and the urine examined at this time showed the presence of the drug upon the application of the ferric chloride test. At noon, on the following day, the patient reported himself as entirely well.

Case II.—Female, æt. 60, suffering from frequently-recurrent and severe rheumatic pains in the shoulder. The method of treatment used in the preceding case was here employed, and the patient reported marked relief on the following day, at which time, also, the drug was found in her urine.

Case III.—Female, æt. 28. Rheumatic pains in arm and shoulder. Application as in previous cases. The drug here proved a decided irritant to the very sensitive skin, and was removed in some fifteen hours. Results negative. Urine not examined. Pain and stiffness subsequently disappeared after the exhibition of large doses of sodium salicylate internally.

Case IV.—Male, æt. 25, frequently subject to rheumatism in the left shoulder, and always relieved by the internal use of sodium salicylate; was

relieved during a similar attack by the method already described.

CASE V.—Male, æt. 34, suffering with severe rheumatic pains in left shoulder.

Thirty grains of salicylic acid were rubbed up in olive oil, gently smeared upon the left side of the abdomen, and covered with rubber-cloth. Here, as in the other cases, the urine was tested for the drug in question at the time that the application was made, with negative results. Urine passed in one hour and ten minutes thereafter gave, upon the application of the ferric chloride test, the response characteristic of the presence of salicylic acid; and this reaction was observed in several samples of urine from this patient up to the thirty-sixth hour after the application was made. In twelve hours the rheumatic symptoms were greatly relieved, and they entirely disappeared within twenty-four hours.

CASE VI.[1]—Dr. F., æt. 29. Rheumatic swelling of right knee, the circumference of which was one-third greater than that of its fellow. Patient gave history of previous persistent rheumatic at-

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[1] We are indebted for the report of this case to the courtesy of Dr. William Gray, who pursued the method indicated at our suggestion.

tacks. Salicylic acid and oil (ʒij to fʒj) were spread upon absorbent cotton, and the whole gently wrapped around the knee, which was here too acutely sensitive to permit of any friction. No internal medication was used. In twenty-four hours there was marked reduction both of pain and swelling, and within three days the patient had entirely recovered. During the treatment, swelling commenced in the knee of the opposite side, but disappeared under the same local treatment pursued with the joint first affected. The urine was several times examined during the treatment, and salicylic acid found therein.

This case is of especial interest as indicating that, superadded to the constitutional impress of the drug, there was a specific local effect at the place of its application.

We do not consider that the results of the six experiments here cited would warrant us in an unqualified commendation of this method of exhibiting salicylic acid, but we feel fully justified in suggesting that a fair trial be given it by the medical profession.

[The following brief statements summarize the results of some of our experiments upon Cutaneous Absorption, which are as yet unpublished.

In general, drugs in solution in oil (not oleates) are absorbed by the normal human skin with greater or less ease. On the other hand, drugs in aqueous solution are not so absorbed. Thus we have shown that salicylic acid in oil is absorbed by the healthy skin, whereas in the similar application of salicylate of sodium, which is practically insoluble in oil, we have never been able to obtain evidence of cutaneous absorption.

In this connection may be mentioned the fact, which we believe has not hitherto been recorded, that methyl salicylate (true oil of wintergreen) is *apparently* absorbed by the human skin. If this oil be gently rubbed over the arm, the presence of salicylic acid in the urine is readily demonstrable at the end of an hour after the application. We say apparently absorbed, because the salicylate in question is volatile, and consequently may be absorbed by the lung surface. A series of control experiments was instituted to determine this point. A little pledget of cotton, saturated with oil of wintergreen, was suspended immediately beneath the nostrils in such wise that it did not come in contact with the skin. The urine, which was found to be free from salicylic acid at the beginning of the experiments, constantly showed the presence of this

drug in from forty to fifty minutes thereafter. The possibility exists that the specific therapeutic impress of salicylic acid may be obtained by inhaling an atmosphere impregnated with this volatile salicylate. We hope to report upon this point in the near future.

The obstacles which prevent the cutaneous absorption of drugs in aqueous solution are the resistant epiderm, and, much more important, the secretion of the sebaceous glands. A very simple and efficacious method which we have devised for removing these obstacles consists in the addition of a proteolytic ferment to the solution of the drug used. Thus trypsin (prepared by Kühne's method) is added to a strong solution of (*e.g.*) morphia. Absorbent cotton is saturated with the mixture, placed upon the skin, and covered over with waterproof plaster. The natural warmth of the part induces the activity of the ferment and the consequent solution of the epiderm, narcosis supervening in from one to two hours. This method, when applied under the supervision of the physician, affords one advantage over ordinary modes of medication, namely, that when the desired therapeutic effect is obtained, the further absorption of the drug may be prevented by at once removing the external application.]